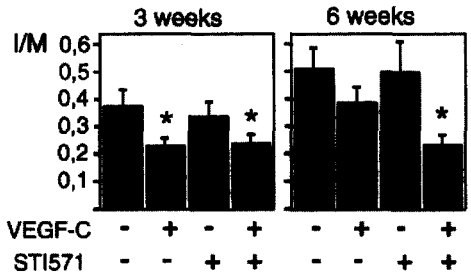
placebo treated control) in intima/media ratio paralleled by accelerated endothelial coverage and reduced intimal cell number.

Conclusions: The combination treatment with VEGF-C adenovirus and STI571 led to a long-lasting inhibition of intimal thickening. Our study is one of the first successful examples of gene therapy combined with pharmacological treatment and provides a novel principle to prevent intimal hyperplasia after vascular intervention.

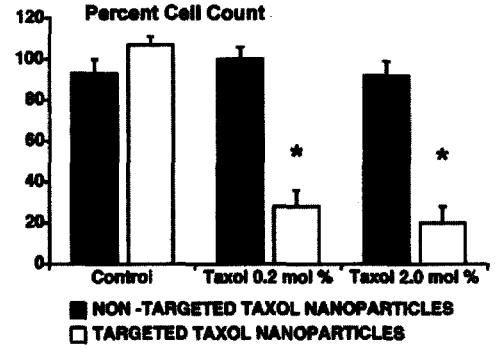


4:30 p.m.

872-3 **Novel Tissue Factor Targeted Therapy Inhibits Vascular Smooth Muscle Cell Proliferation**

Gregory M. Lanza, Dana R. Abendschein, Michael J. Scott, Ralph W. Fuhrhop, David E. Scherrer, Kerry Karukstis, Samuel A. Wickline, *Washington University, St. Louis, Missouri, Harvey Mudd College, Claremont, California.*

Stent-based antiproliferative delivery systems create high lumen drug concentrations in order to achieve therapeutic dosage levels within the tunica media. .High intima drug levels of antiproliferative agents induce inflammation, impede endothelial regrowth, and delay arterial wall healing. We have developed a tissue factor (TF)-targeted paramagnetic nanoparticle that specifically binds to vascular smooth muscle cells (VSMC) and provides local antiproliferative drug delivery. Methods: Anti-tissue factor (TF) nanoparticles incorporating 0 mol%, 0.2mol% or 2.0 mol% paclitaxel or doxorubicin were targeted to VSMC in vitro for 30 minutes and cellular proliferation was determined 3 days later. Results: VSMC proliferation was decreased ($p<0.05$) 0%, 75% and 81% by TF-targeted paclitaxel nanoparticles (Fig) and by 0%, 59% and 72% for TF-targeted doxorubicin nanoparticles, respectively. Effective drug delivery depended on the interaction of the drug-laden nanoparticle surface with the target cell membrane, which was facilitated by the ligand-surface attachments.



Conclusion: TF-targeted paramagnetic nanoparticles can be employed to directly deliver antiproliferative therapy to VSMC in a new clinical paradigm that could circumvent the deleterious side-effects often associated with drug-eluting stent-based approaches.

4:45 p.m.

872-4 **Decorin Overexpression In the Arterial Wall Prevents Neointima Formation and Collagen Accumulation Following Balloon Angioplasty**

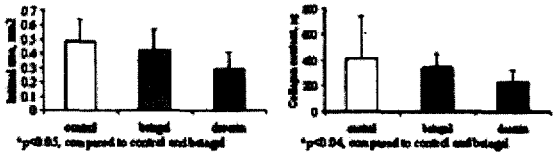
Asim N. Cheema, Nafiseh Nili, Alan W. Barolet, Jacek Linde, Beiping Qiang, Mohammad R. Eskandarian, Frank J. Giordano, John Sparkes, Bradley H. Strauss, *St. Michael's Hospital, Toronto, Ontario, Canada.*

Extracellular matrix (ECM) plays a critical role in the development of restenosis after balloon angioplasty (BA). Collagen is the major ECM protein and its accumulation is an important mechanism of restenosis. In-vitro studies from our laboratory have shown that decorin, a small proteoglycan, inhibits collagen synthesis in cultured smooth muscle cells. Therefore, we evaluated the in-vivo effects of decorin overexpression in the vessel wall.

BA was performed in a double injury model of restenosis in rabbit carotid arteries. Adenoviral-DNA constructs encoding for either betagalactosidase (ß-gal) or decorin were administered intraluminally at the time of 2nd injury. A third group (control) only received 2 balloon injuries without gene transfection. Animals were sacrificed at 10 weeks after 2nd injury. The treated arteries (n=12 per group) were removed and analyzed for collagen content and by morphometry.

The intimal area (mean±SD, mm^2) of decorin group was 0.29±0.12 compared to 0.42±0.14 in the ß-gal and 0.48±0.16 in the control group ($p<0.05$, compared to control and ß-gal). Total collagen content (mean±SD, µg/OH proline per arterial segment) in the decorin group was 228±98 compared to 343±109 in the ß-gal and 411±331 in the control group ($p<0.04$, compared to control and ß-gal).

Adenoviral mediated decorin overexpression inhibits neointima formation and collagen accumulation after balloon injury. These findings suggest a possible therapeutic role for decorin in the treatment of restenosis after BA.



ORAL CONTRIBUTIONS

880 Intravascular Ultrasound, Drug Coated Stents, and Vascular Brachytherapy

Wednesday, March 20, 2002, 8:30 a.m.-10:00 a.m.
Georgia World Congress Center, Room 264W

8:30 a.m.

880-1 **Three-Dimensional IVUS Assessment of Edge Effects Following Drug-Eluting Stent Implantation**

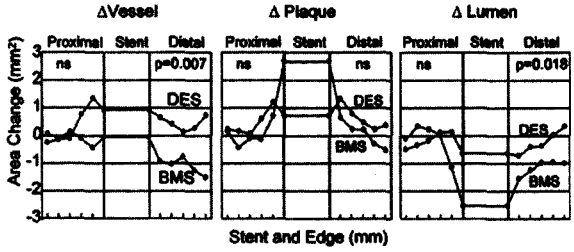
Toru Kataoka, Eberhard Grube, Yasuhiro Honda, Karl E. Hauptmann, Yoshihiro Morino, Seung-Ho Hur, Paul G. Yock, Peter J. Fitzgerald, SCORE investigators group, *Stanford University, Stanford, California, Heart Center Siegburg, Siegburg, Germany.*

Drug-eluting stents produce a striking reduction of neointimal growth within the stent. However, potential edge effects have not been systematically investigated. The purpose of this study was to use serial 3-D IVUS to evaluate the long-term vessel response at adjacent reference segments of the QUANAM QP2 (a taxol analogue)-eluting stent (DES) compared to bare metal stents (BMS).

Methods: Serial (baseline and 6-month follow-up) IVUS images of 69 stent edges in 40 patients (20 DES; 20 BMS) were analyzed in SCORE, a randomized trial comparing DES vs. BMS. External elastic membrane (EEMA), plaque (PA), and lumen areas (LA) were measured at every 1 mm cross-section within 5 mm outside of both stent margins. Area changes (Δ) were computed as follow-up minus baseline.

Results: Baseline lesion and procedural characteristics were similar in the two groups. Overall, DES had a slightly greater mean ΔPA at the stent edges than BMS (DES 0.63±1.35 vs BMS 0.03±1.01 mm^2, p=0.04). However, mean ΔLA was similar in the two groups (DES -0.31±1.25 mm^2 vs BMS -0.63±1.31 mm^2, ns) due to an increase in mean EEMA in DES (ΔEEMA: DES 0.35±1.51 vs BMS -0.60±1.51 mm^2, p=0.01). Figure shows ΔEEMA, ΔPA, and ΔLA over the stent edges.

Conclusions: This 3-D IVUS analysis of SCORE revealed no evidence of negative edge effects following the QP2-eluting stent implantation as compared to bare metal stents. The preservation of edge lumen with the QP2-eluting stent was due to a prevention of vessel shrinkage, particularly at the distal reference.



8:45 a.m.

880-2 **Edge Effect Does Not Occur After Implantation of Sirolimus-Eluting Stents: A Three-Dimensional Intravascular Ultrasound Analysis From the RAVEL Trial**

Andrea S. Abizaid, J. Eduardo Sousa, Pim de Feyter, Alexandre Abizaid, Egon Wuelfert, William Wijns, Marie C. Morice, Giulio Guagliumi, Antonio Colombo, Patrick Serruys, *Institute Dante Pazzanese of Cardiology, Sao Paulo, Brazil, Lenox Hill Heart and Vascular Institute, Cardiovascular Research Foundation, New York, New York.*

Background: Edge lumen loss, the so-called "edge effect,' is one of the limitations of brachytherapy, especially after implanting beta-emitting stents. The purpose of the current analysis is to determine whether edge effects also occur after implantation of sirolimus-eluting stents. **Methods:** The RAVEL trial, a placebo-controlled randomized multicenter study, compared sirolimus-eluting (SE) Bx Velocity™ stents (Cypher™) versus uncoated Bx Velocity™ stents in 237 pts with single, de novo lesions in native coronary arteries. All patients received clopidogrel for a 2-month period. Serial volumetric intravascular ultrasound (IVUS) analysis was performed in 95 patients at 6 months follow-up. The volumetric analysis included 5mm long reference segments adjacent to the proximal and distal edges of the stent. Mean cross-sectional area results over the length of the reference segments are reported. **Results:** In pts treated with SE stents, there was